ONLINE EXCLUSIVE

Lawrence M. Gibbs, MD, MSEd; Rajasree J. Nair, MD
Methodist Charlton Family Medicine Residency, Dallas, TX

Joan Nashelsky, MLS
Family Physicians Inquiries Network, Iowa City

ASSISTANT EDITOR
Rick Guthmann, MD, MPH
Advocate Illinois Masonic Family Medicine Residency, Chicago

Q/ Does evidence support the use of supplements to aid in BP control?

EVIDENCE-BASED ANSWER

A/ **Yes.** A number of well-tolerated natural therapies have been shown to reduce systolic and diastolic blood pressure (BP). (See **TABLE**[1-8] for summary.) However, the studies don't provide direct evidence of whether the decrease in BP is linked to patient-oriented outcomes. Nor do they allow definitive conclusions concerning the lasting nature of the reductions, because most studies were fewer than 6 months in duration (strength of recommendation: **C**, disease-oriented evidence).

Evidence summary

Cocoa. A 2017 Cochrane review evaluated data from more than 1800 patients (401 in hypertension studies) to determine the effect of cocoa on BP.[1] Compared with placebo (in flavanol-free or low-flavanol controls), cocoa lowered systolic BP by 1.8 mm Hg (confidence interval [CI], –3.1 to –0.4) and diastolic BP by 1.8 mm Hg (CI, –2.6 to –0.9). Further analysis of patients with hypertension (only) showed a reduction in systolic BP of 4 mm Hg (CI, –6.7 to –1.3).

Omega-3 fatty acids. Similarly, a 2014 meta-analysis investigating omega-3 fatty acids (eicosapentaenoic acid [EPA] + docosahexaenoic acid [DHA]) included data from 4489 patients (956 with hypertension) and showed reductions in systolic BP of 1.5 mm Hg (CI, –2.3 to –0.8) and diastolic BP of 1 mm Hg (CI, –1.5 to –0.4), compared with placebo.[2] Again, subgroup analysis of patients with hypertension (only) at baseline revealed a greater decrease in systolic and diastolic BP: 4.5 mm Hg (CI, –6.1 to –2.8) and 3.1 mm Hg (CI, –4.4 to –1.8), respectively.

Garlic and potassium chloride. Separate meta-analyses that included only patients with hypertension found that both garlic and potassium significantly lowered BP.[3,4] A 2015 meta-analysis comparing a variety of garlic preparations with placebo in patients with hypertension showed decreases in systolic BP of 9.1 mm Hg (CI, –12.7 to –5.4) and in diastolic BP of 3.8 mm Hg (CI, –6.7 to –1).[3] Meanwhile, a meta-analysis in 2017 comparing different doses of potassium chloride with placebo demonstrated reductions in systolic BP of 4.3 mm Hg (CI, –6 to –2.5) and diastolic BP of 2.5 mm Hg (CI, –4.1 to –1).[4]

L-arginine. Another meta-analysis of randomized controlled trials reported evidence that oral L-arginine, compared with placebo, significantly reduced systolic BP by 5.4 mm Hg (CI, –8.5 to –2.3) and diastolic BP by 2.7 mm Hg (CI, –3.8 to –1.5).[5] Close to one-third of patients had hypertension at baseline.

Beetroot juice. A double-blind, placebo-controlled study showed that consumption of beetroot juice (with nitrate) once daily reduced BP in 3 different settings (clinic, 24-hour ambulatory, and home readings) when compared with placebo (nitrate-free beetroot juice).[6] Study participants were mostly British women, overweight, without significant cardiovascular or renal disease, and with uncontrolled ambulatory BP (> 135/85 mm Hg).

Flax seed. A prospective, double-blind trial of patients with peripheral artery disease compared the antihypertensive effects

TABLE

How well do these supplements aid in BP control?

Therapy (study type)	Subjects	Dose	Duration (wk)	Adverse effects	Effect on BP, reduction in mm Hg	Comments
Beetroot/ nitrate[6] (RCT)	68 (all with HTN; half drug naïve and half medication treated)	Beetroot juice 250 mL/d (~ 6.4 mmoL nitrate)	4	Beeturia and fecal discoloration (mild)	Mean: SBP = 7.7 (CI, –11.8 to –3.6; $P < .001$) DBP = 2.4 (CI, –4.9 to 0.0; $P = .050$) 24-hr BP: SBP = 7.7 (CI, –11.2 to –4.1; $P < .001$) DBP = 5.2 (CI, –7.7–-2.7; $P < 0.001$) Home BP: SBP = 8.1 (CI, –12.4 to –3.8; $P < .001$) DBP = 3.8 (CI, –6.9 to –0.7; $P < .01$)	No nitrate-associated tachyphylaxis was noted
Cocoa[1] (SR/MA)	1804 (401 with HTN)	1.4-105 g/d of cocoa products	2-18 (mean, 9)	Mild GI symptoms including nausea	SBP = 1.8 (CI, –3.1 to –0.4) DBP = 1.8 (CI, –2.6 to –0.9) HTN subgroup: SBP = 4 (CI, –6.7 to –1.3) DBP N/A	Moderate-quality evidence; moderate-high heterogeneity; mild reporting bias
Flax seed[7] (prospective RCT)	110 (all with HTN)	30 g/d	24	Similar to placebo	SBP = 10 ($P = .04$) DBP = 7 ($P = .004$)	All patients had PAD; BP reductions were more pronounced in patients with HTN
Garlic[3] (SR/MA, 9 RCTs)	482 (all with HTN)	240-2400 mg/d (aged extract, garlic oil, garlic powder, egg yolk–enriched garlic powder)	8-26 (mean, 13.5)	Mild GI symptoms such as burping, flatulence, and reflux	SBP = 9.1 (CI, –12.7 to –5.4; $P = .0006$) DBP = 3.8 (CI, –6.7 to –1; $P = .00001$)	Quality of included trials was moderate; moderate-high heterogeneity; insufficient data to determine publication bias
L-arginine[5] (SR/MA, 11 RCTs)	387 (1/3 with baseline HTN)	4-24 g/d (mean, 9 g/d)	2-24 (mean, 4)	Diarrhea	SBP = 5.4 (CI, –8.5 to –2.3; $P = .001$) DBP = 2.7 (CI, –3.8 to –1.5; $P < .001$)	All studies were double-blind; BP primary outcome in 5 studies; moderate heterogeneity; greater BP reduction in patients with higher baseline BP
Olive leaf[8] (RCT)	148 (all with HTN)	Olive leaf extract 500 mg bid; captopril 12.5-25 mg	8	Cough, vertigo, myalgias, and headache (mild and similar between groups)	Olive leaf extract: SBP = 11.5 ± 8.6 DBP = 4.8 ± 5.5 Captopril: SBP = 13.7 ± 7.6 DBP = 6.4 ± 5.2 (Difference between treatments $P > .05$)	Study excluded patients with signs of target organ damage (eg, heart, kidneys, liver)

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TABLE

How well do these supplements aid in BP control? (*cont'd*)

Therapy (study type)	Subjects	Dose	Duration (wk)	Adverse effects	Effect on BP, reduction in mm Hg	Comments
Omega-3 fatty acids (EPA+DHA)[2] (SR/MA, 70 RCTs)	4489 (956 with HTN)	EPA+DHA dose: 0.1-15 g/d (mean, 3.8 g/d)	4-52 (mean, 10)	NR	Overall: SBP = 1.5 (CI, –2.3 to –0.8) DBP = 1 (CI, –1.5 to –0.4) HTN subjects: SBP = 4.5 (CI, –6.1 to –2.8) DBP = 3.1 (CI, –4.4 to –1.8)	All trials were double-blind; low heterogeneity; mild publication bias
Potassium[4] (SR/MA, 23 RCTs)	1213 (all with HTN)	6-200 mEq of KCl daily	4-52	Abdominal pain, nausea, vomiting, diarrhea, gas. (mild, similar to placebo)	SBP = 4.3 (CI, –6.0 to –2.5; $P < .00001$) DBP = 2.5 (CI, –4.1 to –1.0; $P < .001$) Mean change data: SBP = 8.9 (CI, –13.7 to –4.1; $P = .0003$); DBP = 6.4 (CI, –11 to –1.8; $P = .006$)	Mild-moderate heterogeneity; low bias; showed dose-response relationship

BP, blood pressure; CI, 95% confidence interval; DBP, diastolic blood pressure; EPA+DHA, eicosapentaenoic acid + docosahexaenoic acid; GI, gastrointestinal; HTN, hypertension; KCl, potassium chloride; NA, not available; NR, not reported; PAD, peripheral artery disease; RCT, randomized controlled trial; SBP, systolic blood pressure; SR/MA, systematic review and meta-analysis.

of flax seed with placebo in patients with and without hypertension and found marked decreases in systolic and diastolic BP.[7] Study participants were all older than 40 years without other major cardiac or renal disease, and the majority of enrolled patients with hypertension were concurrently taking medications to treat hypertension during the study.

Olive leaf extract. A double-blind, parallel, and active-control clinical trial in Indonesia compared the BP-lowering effect of olive leaf extract (*Olea europaea*) to captopril as monotherapies in patients with stage 1 hypertension.[8] After a 4-week period of dietary intervention, individuals who were still hypertensive (range, 140/90 to 159/99 mm Hg) were treated with either olive leaf extract or captopril. After 8 weeks of treatment, both groups saw comparable reductions in BP.

Editor's takeaway

Many studies have demonstrated BP benefits from a variety of natural supplements. Although the studies' durations are short, the effects sometimes modest, and the outcomes disease-oriented rather than patient-oriented, the findings can provide a useful complement to our efforts to manage this most common chronic disease. JFP

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